

## Abstract

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### Vertical transmission of coronavirus disease 2019: a systematic review and meta-analysis

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**Objective:** This study aimed to conduct a systematic review of the current literature to determine estimates of vertical transmission of coronavirus disease 2019 based on early RNA detection of severe acute respiratory syndrome coronavirus 2 after birth from various neonatal or fetal sources and neonatal serology.

**Study Eligibility Criteria:** This systematic review included cohort studies, case series, and case reports of pregnant women who received a coronavirus disease 2019 diagnosis using severe acute respiratory syndrome coronavirus 2 viral RNA test and had reported data regarding the testing of neonates or fetuses for severe acute respiratory syndrome coronavirus 2 immediately after birth and within 48 hours of birth. A total of 30 eligible case reports describing 43 tested neonates and 38 cohort or case series studies describing 936 tested neonates were included.

**Study Appraisal and Synthesis Methods:** The methodological quality of all included studies was evaluated by a modified version of the Newcastle-Ottawa scale. Quantitative synthesis was performed on cohort or case series studies according to the neonatal biological specimen site to reach pooled proportions of vertical transmission.

**Results:** Our quantitative synthesis revealed that of 936 neonates from mothers with coronavirus disease 2019, 27 neonates had a positive result for severe acute respiratory syndrome coronavirus 2 viral RNA test using nasopharyngeal swab, indicating a pooled proportion of 3.2% (95% confidence interval, 2.2–4.3) for vertical transmission. Of note, the pooled proportion of severe acute respiratory syndrome coronavirus 2 positivity in neonates by nasopharyngeal swab in studies from China was

2.0% (8/397), which was similar to the pooled proportion of 2.7% (14/517) in studies from outside of China. Severe acute respiratory syndrome coronavirus 2 viral RNA testing in neonatal cord blood was positive in 2.9% of samples (1/34), 7.7% of placenta samples (2/26), 0% of amniotic fluid (0/51), 0% of urine samples (0/17), and 9.7% of fecal or rectal swabs (3/31). Neonatal serology was positive in 3 of 82 samples (3.7%) (based on the presence of immunoglobulin M).

**Conclusion:** Vertical transmission of severe acute respiratory syndrome coronavirus 2 is possible and seems to occur in a minority of cases of maternal coronavirus disease 2019 infection in the third trimester. The rates of infection are similar to those of other pathogens that cause congenital infections. However, given the paucity of early trimester data, no assessment can yet be made regarding the rates of vertical transmission in early pregnancy and potential risk for consequent fetal morbidity and mortality.

### Early preterm preeclampsia outcomes by intended mode of delivery

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**Objective:** Objective was to investigate labor induction success rates and compare maternal and neonatal outcomes by intended mode of delivery in women with early preterm preeclampsia.

**Materials & methods:** We identified 914 singleton pregnancies with preeclampsia in the Consortium on Safe Labor study for analysis who delivered between 24 0/7 and 33 6/7 weeks. We excluded fetal anomalies, antepartum stillbirth, or spontaneous preterm labor. Maternal and neonatal outcomes were compared between women undergoing induction of labor (n = 460) and planned cesarean delivery (n = 454) and women with successful induction of labor (n = 214) and unsuccessful induction of labor (n = 246). We calculated relative risks and 95% confidence intervals to determine outcomes by Poisson regression model with propensity score

adjustment. The calculation of propensity scores considered covariates such as maternal age, gestational age, parity, body mass index, tobacco use, diabetes mellitus, chronic hypertension, hospital type and site, birthweight, history of cesarean delivery, malpresentation/breech, simplified Bishop score, insurance, marital status, and steroid use.

**Results:** Among the 460 women with induction (50%), 47% of deliveries were vaginal. By gestational age, 24 to 27 6/7, 28 to 31 6/7, and 32 to 33 6/7, the induction of labor success rates were 38% (12 of 32), 39% (70 of 180), and 54% (132 of 248), respectively. Induction of labor compared with planned cesarean delivery was less likely to be associated with placental abruption (adjusted relative risk, 0.33; 95% confidence interval, 0.16-0.67), wound infection or separation (adjusted relative risk, 0.23; 95% confidence interval, 0.06-0.85), and neonatal asphyxia (0.12; 95% confidence interval, 0.02-0.78). Women with vaginal delivery compared with those with failed induction of labor had decreased maternal morbidity (adjusted relative risk, 0.27; 95% confidence interval, 0.09-0.82) and no difference in neonatal outcomes.

**Conclusion:** About half of women with preterm preeclampsia who attempted an induction had a successful vaginal delivery. The rate of successful vaginal delivery increases with gestational age. Successful induction has the benefit of preventing maternal and fetal comorbidities associated with previous cesarean deliveries in subsequent pregnancies. While overall rates of a composite of serious maternal and neonatal morbidity/mortality did not differ between induction of labor and planned cesarean delivery groups, women with failed induction of labor had increased maternal morbidity highlighting the complex route of delivery counseling required in this high-risk population of women.

**Primary cytomegalovirus infection during pregnancy and subsequent congenital infection: maternal antibody screening involving 19,000 women**

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**Objective:** To identify the incidence rates of primary cytomegalovirus (CMV) infection during pregnancy and subsequent congenital CMV infection in Japan by conducting a maternal CMV antibody screening

program in a large population of Mie Prefecture, Japan.

**Materials & methods:** We performed a population-based, observational, prospective cohort study. Women in early pregnancy were registered and tested for both CMV IgG and IgM antibodies. For the pregnant women who had positive results for both IgG and IgM antibodies, the IgG avidity index was measured. Those who had negative IgG antibody results were instructed by their obstetricians to take preventive measures against primary infection during pregnancy. Then, the women were retested for both IgG and IgM antibodies at late pregnancy. Primary infections were considered in the following two antibody screening results: one was positive IgG antibody, positive IgM antibody, and low IgG avidity index, and the other was IgG antibody seroconversion at late pregnancy from negative IgG antibody results at early pregnancy. For the pregnant women with primary infection, CMV DNA tests were performed for congenital infection.

**Results:** From September 2013 to March 2017, 19,435 pregnant women were registered in 24 centers in Mie Prefecture, Japan. Of 1,037 pregnant women with both positive IgG and IgM results, 115 showed a low IgG avidity index and were considered as having a primary infection. Of 6,636 pregnant women with negative IgG results at early pregnancy, only 4,082 were retested for IgG and IgM antibodies at late pregnancy, as 2,554 women had missing data. Of the 4,082 pregnant women with negative IgG results at early pregnancy, 31 showed IgG antibody seroconversion at late pregnancy and were considered as having a primary infection. Twenty-three women delivered a fetus with a congenital infection; 8 of 115 women had low IgG avidity index, and 15 of 31 women had IgG seroconversion. The observed incidence rates of primary and subsequent congenital infections were 0.75% and 0.12%, respectively (115 + 31 primary infection and 8 + 15 congenital infection, respectively). The estimated rates that the missing data were corrected were 0.85% and 0.16%, respectively (115 + 50 primary infection and 8 + 24 congenital infection, respectively).

**Conclusion:** The incidence rates of primary CMV infection during pregnancy and subsequent congenital CMV infection in Japan were estimated to be 0.85% and 0.16%, respectively.

## COVID-19 (SARS-CoV-2) Infection in Pregnancy: A Systematic Review

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**Objectives:** To review published studies related to the association of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections with pregnancy, foetal, and neonatal outcomes during coronavirus disease 2019 (COVID-19) pandemic in a systematic manner.

**Methods:** A comprehensive electronic search was done through PubMed, Scopus, Medline, Cochrane database, and Google Scholar from December 01, 2019, to May 22, 2020, along with the reference list of all included studies. All cohort studies that reported on outcomes of COVID-19 during pregnancy were included. Qualitative assessment of included studies was performed using the Newcastle-Ottawa scale.

**Results:** Upon admission, most pregnant women underwent a low-dose radiation CT scan; the reports of which included unilateral/bilateral pneumonia in

most patients. A marked lymphopenia was also noted in many patients with COVID-19. 513 titles were screened, and 22 studies were included, which identified 156 pregnant women with COVID-19 and 108 neonatal outcomes. The most common maternal/foetal complications included intrauterine/foetal distress (14%) and premature rupture of membranes (8%). The neonatal clinical manifestations of COVID-19 commonly included shortness of breath (6%), gastrointestinal symptoms (4%), and fever (3%).

**Conclusion:** COVID-19 infection in pregnancy leads to increased risk in pregnancy complications such as preterm birth, PPRM, and may possibly lead to maternal death in rare cases. There is no evidence to support vertical transmission of SARS-CoV-2 infection to the unborn child. Due to a paucity of inconsistent data regarding the impact of COVID-19 on the newborn, caution should be undertaken to further investigate and monitor possible infection in the neonates born to COVID-19-infected mothers.